

Attorney Docket No. PP00338.105 (2300-0338.02)

PATENT

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to the Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on 3/16/04.

By: 

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of PIZZA et al.

Serial No.: 10/611,398

Examiner: Not Assigned

Confirmation No.: 1890

Art Unit: 1642

Filed: June 30, 2003

For: IMMUNOGENIC DETOXIFIED MUTANTS OF CHOLERA TOXIN

---

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

### INFORMATION DISCLOSURE STATEMENT TRANSMITTAL

Enclosed is an Information Disclosure Statement and accompanying Form PTO/SB/08A for the above-identified patent application.

- ☒ In accordance with 37 C.F.R. §1.97(b), no additional fee for submission of the IDS is required.
- ☐ In accordance with 37 C.F.R. §1.97(c), also enclosed is:
- ☐ the fee of \$180.00 as set forth in 37 C.F.R. §1.17(p); or
  - ☐ a statement as specified in 37 C.F.R. §1.97(e).
- ☐ In accordance with 37 C.F.R. §1.97(d), a statement as specified in 37 C.F.R. §1.97(e) and the fee of \$180.00 as set forth in 37 C.F.R. §1.17(p) are also enclosed.
- ☐ Check No. \_\_\_\_ in the amount of \$\_\_\_\_ for the total fee is attached.

☒ [X] A return receipt postcard is also enclosed.

☐ [] Please charge \$\_\_\_\_\_ to Deposit Account No. 18-1648 for the total fee.  
This paper is being submitted in duplicate.

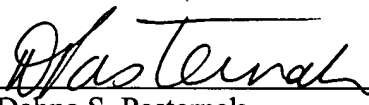
The Commissioner is hereby authorized to charge any appropriate fees under 37 C.F.R. §§1.16, 1.17, and 1.21 that may be required by this paper, and to credit any overpayment, to Deposit Account No. 18-1648.

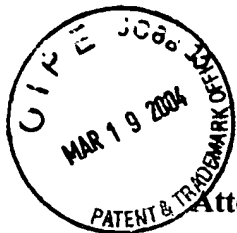
Dated: March 15, 2004

Respectfully submitted,

Chiron Corporation  
Intellectual Property – R440  
PO Box 8097  
Emeryville, CA 94662-8097  
Tel: (650) 493-3400  
Fax: (650) 493-3440

By:

  
Dahna S. Pasternak  
Reg. No. 41,411



Attorney Docket No. PP00338.105 (2300-0338.02)

PATENT

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to the Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on 3/16/04

By: 

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of PIZZA et al.

Serial No.: 10/611,398

Examiner: Not Assigned

Confirmation No.: 1890

Art Unit: 1642

Filed: June 30, 2003

For: IMMUNOGENIC DETOXIFIED MUTANTS OF CHOLERA TOXIN

---

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

### INFORMATION DISCLOSURE STATEMENT UNDER 37 C.F.R. §1.97(b)

In accordance with the duty of disclosure set forth in 37 C.F.R. §1.56,  
Applicant(s) hereby submits the following information in conformance with 37 C.F.R.  
§§1.97 and 1.98.

- ☐ Pursuant to 37 C.F.R. §1.98, a copy of each document cited in the attached Form PTO/SB/08 is enclosed.
- ☒ No copies of the publications listed on the attached Form PTO/SB/08A are being provided pursuant to 37 C.F.R. §1.98(d) because the publications were previously cited by or submitted to the Office in prior Application Serial No. 09/819,917 to which the above-identified application claims priority under 35 U.S.C. §120.
- ☐ Publication(s) \_\_\_\_\_ listed on the attached Form PTO/SB/08A were cited in a foreign search or examination report corresponding to \_\_\_\_\_ application serial no. \_\_\_\_\_ and mailed on \_\_\_\_\_.

- ☐ Enclosed is a copy of a non-English publication(s) \_\_\_\_\_. Pursuant to §609 of the M.P.E.P., Applicant submits the attached foreign search or examination report, which cites such non-English language publication(s).
- ☐ Enclosed is a copy of a non-English publication(s) \_\_\_\_\_. English language publication \_\_\_\_\_ (copy enclosed) claims priority from this non-English publication.
- ☐ Enclosed is an explanation of non-English publication(s) \_\_\_\_\_ for which an English translation is not available.
- ☐ Enclosed is an English translation of non-English publication(s) \_\_\_\_\_ cited in the attached Form PTO/SB/08A.
- ☐ Enclosed is a copy of pending patent Application Serial No. \_\_\_\_\_.

This Information Disclosure Statement is filed within any one of the following time periods:

- ☐ within three months from the filing date of this national application other than a CPA under 37 C.F.R. § 1.53(d);
- ☐ within three months from the date of entry of the national stage as set forth in 37 C.F.R. §1.491 in this international application;
- ☒ before the mailing date of a first office action on the merits; or
- ☐ before the mailing of a first office action after the filing of a request for continued examination under 37 C.F.R. §1.114.

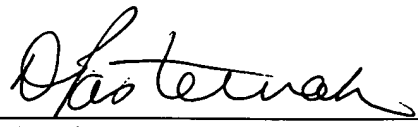
It is respectfully requested that the Examiner consider the above-noted information and return an initialed copy of the attached Form PTO/SB/08A to the undersigned.

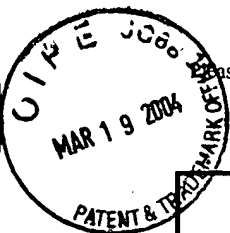
Dated: 3-15-04

Respectfully submitted,

Chiron Corporation  
Intellectual Property – R440  
PO Box 8097  
Emeryville, CA 94662-8097  
Tel: (650) 493-3400  
Fax: (650) 493-3440

By:

  
Dahna S. Pasternak  
Reg. No. 41,411



Please type a plus sign (+) inside this box →



PTO/SB/08A (08-00)

<b>Substitute for form 1449A/PTO</b>  <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (use as many sheets as necessary)				<b>Complete if Known</b>	
				Application Number	10/611,398 (Confirmation No. 1890)
				Filing Date	June 30, 2003
				First Named Inventor	PIZZA et al.
				Group Art Unit	1642
				Examiner Name	Unassigned
Sheet	1	of	3	Attorney Docket Number	PP00338.105 (2300-0338.02)

U.S. PATENT DOCUMENTS					
Examiner Initials*	Cite No. <sup>1</sup>	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY
		Number	Kind Code <sup>2</sup> (if known)		
	A1	4,328,209		Finkelstein et al.	5/4/82
	A2	4,666,837		Harford et al.	5/19/87
	A3	4,935,364		Kaper et al.	6/19/90
	A4	5,601,827		Collier et al.	2/11/97
	A5	5,668,255		Murphy	9/16/97
	A6	5,770,203		Burnette et al.	6/23/98
	A7	6,019,982		Clements et al.	2/1/00
	A8	6,033,673		Clements	3/7/00
	A9	6,149,919		Domenighini et al.	11/00

FOREIGN PATENT DOCUMENTS							
Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document			Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	T <sup>6</sup>
		Office <sup>3</sup>	Number <sup>4</sup>	Kind Code <sup>5</sup> (if known)			
	B1	WO	92/19265			11/12/92	
	B2	WO	93/13202		Domenighini	7/8/93	

Examiner Signature		Date Considered	
--------------------	--	-----------------	--

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Unique citation designation number.

<sup>2</sup> See attached Kinds of U.S. Patent Documents.

<sup>3</sup> Unique citation designation number.

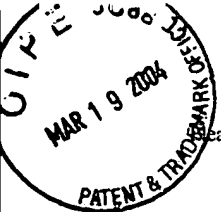
<sup>4</sup> See attached Kinds of U.S. Patent Documents.

<sup>5</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3).

<sup>6</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.

<sup>7</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible.

<sup>8</sup> Applicant is to place a check mark here if English language Translation is attached.



Please type a plus sign (+) inside this box →



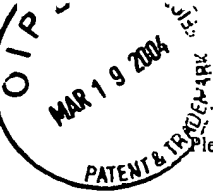
PTO/SB/08A (08-00)

<b>Substitute for form 1449A/PTO</b>  <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (use as many sheets as necessary)		<b>Complete if Known</b>			
		<b>Application Number</b>	10/611,398 (Confirmation No. 1890)		
		<b>Filing Date</b>	June 30, 2003		
		<b>First Named Inventor</b>	PIZZA et al.		
		<b>Group Art Unit</b>	1642		
		<b>Examiner Name</b>	Unassigned		
<b>Sheet</b>	2	<b>of</b>	3	<b>Attorney Docket Number</b>	PP00338.105 (2300-0338.02)

OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS		
Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.
	C1	BOSLEGO, J.W. et al., Vaccines and Immunotherapy, Chapter 17, 1991, 211-223
	C2	BURNETTE, W.N. et al., "Site-specific mutagenesis of the catalytic subunit of cholera toxin: substituting lysine for arginine 7 causes loss of activity," <i>Inf. &amp; Immun.</i> , 1991, 59:4266-4270
	C3	DALLAS, W.S. et al., "Cistrons encoding <i>Escherichia coli</i> heat-labile toxin," <i>J. Bacteriol.</i> , 1979, 139:850-858
	C4	DENTE, L. et al., "pEMBL: a new family of single stranded plasmids," <i>Nucleic Acids Res.</i> , 1983 11(6):1645-1655
	C5	DOMENIGHINI, M. et al., "Identification of errors among database sequence entries and comparison of correct amino acid sequences for the heat-labile enterotoxins of <i>Escherichia coli</i> and <i>Vibrio cholerae</i> ," <i>Mol. Microbiol.</i> , 1995, 15(6):1165-1167
	C6	DOMENIGHINI, M. et al., "Common features of the DNA-binding and catalytic site of ADP-ribosylating toxins," <i>Mol. Microbiol.</i> , 1994, 14(1):41-50
	C7	DICKINSON, B. et al., "Dissociation of <i>Escherichia coli</i> heat-labile enterotoxin adjuvant activity from ADP-ribosyltransferase activity," <i>Infection and Immunity</i> , 1995, 63(5):1617-1623
	C8	DONTA, S., "Detection of heat-labile <i>Escherichia coli</i> enterotoxin with the use of adrenal cells in tissue culture," <i>Science</i> , 1974, 183:334-336
	C9	FONTANA, M.R. et al., "Construction of nontoxic derivatives of cholera toxin and characterization of the immunological response against the A subunit," <i>Infection and Immunity</i> , 1995, 63(6):2356-2360
	C10	GRANT, C. et al., "Role of trypsin-like cleavage at arginine 192 in the enzymatic and cytotoxic activities of <i>Escherichia coli</i> heat-labile enterotoxin," <i>Infection and Immunity</i> , 1994, 62(10):4270-4278
	C11	GRANT, C.C.R. et al., "Effect of single amino acid changes on the ADP-ribosyltransferase activity of <i>Escherichia coli</i> heat-labile toxin subunit A," <i>92<sup>nd</sup> Gen. Meet. Am. Soc. Microbiol.</i> , 1992, Abstract B278, 74
	C12	HARFORD, S. et al., "Inactivation of the <i>Escherichia coli</i> heat-labile enterotoxin by in vitro mutagenesis of the A-subunit gene," <i>Eur. J. Biochem.</i> , 1989, 183:311-316
	C13	HASE, C. et al., "Construction and characterization of recombinant <i>Vibrio cholerae</i> strains producing inactive cholera toxin analogs," <i>Infection and Immunity</i> , 1994, 62(8):3051-3057
	C14	HIRST, T. et al., "Transient entry of enterotoxin subunits into the periplasm occurs during their secretion from <i>Vibrio cholerae</i> ," <i>J. Bacteriol.</i> , 1987, 169(3):1037-1045
	C15	HOLMGREN, J. et al., "Oral immunization against cholera," <i>Curr. Top. Microbiol. Immunol.</i> , 1998, 146:197-204
	C16	JOBLING, M.G. et al., "Analysis of the structure and function of cholera toxin A subunit," <i>Abstr. Gen. Meet. Am. Soc. Microbiol.</i> , 1991, 91(0), 59, #B205
	C17	KASLOW, H.R. et al., "Effects of site-directed mutagenesis on cholera toxin A1 subunit ADP-ribosyltransferase activity," <i>92<sup>nd</sup> Gen. Meet. Am. Soc. Microbiol.</i> , 1992, Abstract B291, 74
	C18	KASLOW, H.R. et al., "Site-specific mutagenesis of the pertussis toxin S1 subunit gene: effects of amino acid substitutions involving residues 50-58," <i>Vaccine Research</i> , 1992, 1(1):47-54
	C19	LAI, C.Y. et al., "Location and amino acid sequence around the ADP-ribosylation site in the cholera toxin active subunit A <sub>1</sub> ," <i>Biochem. Biophys. Res. Comm.</i> , 1983, 116:341-348
	C20	<i>The Lancet</i> , September 27, 1986, 328(8509):722-723, "Oral Cholera Vaccines"
	C21	LEBACQ-VERHEYDEN, A.M. et al., "Posttranslation processing of endogenous and of baculovirus-expressed human gastrin-releasing peptide precursor," <i>Mol. Cell. Biol.</i> , 1988, 8:3129-3135
	C22	LOBET, Y. et al., "Effect of site-directed mutagenic alterations on ADP-ribosyltransferase activity of the A subunit of <i>Escherichia coli</i> heat-labile enterotoxin," <i>Inf. &amp; Immun.</i> , 1991, 59:2870-2879
	C23	LOOSEMORE, S.M. et al., "Engineering of genetically detoxified pertussis toxin analogs for development of a recombinant whooping cough vaccine," <i>Infection and Immunity</i> , 1990, 58(11):3653-3662
	C24	LYCKE, N. et al., "The adjuvant effect of <i>Vibrio cholerae</i> and <i>Escherichia coli</i> heat-labile enterotoxins is linked to their ADP-ribosyltransferase activity," <i>Eur. J. Immunol.</i> , 1992, 22:2277-2281

<b>Examiner Signature</b>		<b>Date Considered</b>	
---------------------------	--	------------------------	--

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.



Please type a plus sign (+) inside this box →



PTO/SB/08A (08-00)

<b>Substitute for form 1449A/PTO</b>  <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (use as many sheets as necessary)				<b>Complete if Known</b>	
				Application Number	10/611,398 (Confirmation No. 1890)
				Filing Date	June 30, 2003
				First Named Inventor	PIZZA et al.
				Group Art Unit	1642
				Examiner Name	Unassigned
Sheet	3	of	3	Attorney Docket Number	PP00338.105 (2300-0338.02)

C25	MAGAGNOLI, C. et al., "Mutations in the A subunit affect yield, stability, and protease sensitivity of nontoxic derivatives of heat-labile enterotoxin," <i>Infection and Immunity</i> , 1996, 64(12):5434-5438
C26	MEKALANOS, J.J. et al., "Cholera toxin genes: nucleotide sequence, deletion analysis and vaccine development," <i>Nature</i> , 1983, 306:551-557
C27	<i>Molecular Microbiology</i> , 1995, 15(6):1165-1167, "MicroCorrespondence"
C28	OKAMOTO, J. et al., "Effect of substitution of glycine for arginine at position 146 of the A1 subunit on biological activity of <i>Escherichia coli</i> heat-labile enterotoxin," <i>Bacteriol.</i> , 1988, 2208
C29	OSEASOHN, R., "Cholera," In Plotkin S.A., Mortimer, E.A. (Eds.), <i>Vaccines</i> , 1988, WB Saunders Co., Philadelphia, PA
C30	PEARSON, G. et al., "Molecular cloning of <i>Vibrio cholerae</i> enterotoxin genes in <i>Escherichia coli</i> K-12," <i>Proc. Natl. Acad. Sci. USA</i> , 1982, 79:2976-2980
C31	PICKETT, C.L. et al., "Genetics of type IIA heat-labile enterotoxin of <i>Escherichia coli</i> : operon fusions, nucleotide sequence, and hybridization studies," <i>J. Bacteriol.</i> , 1987, 169:5180-5187
C32	PIZZA, M. et al., "A genetically detoxified derivative of heat-labile <i>Escherichia coli</i> enterotoxin induces neutralizing antibodies against the A subunit," <i>J. Exp. Med.</i> , 1994, 180:2147-2153
C33	PIZZA, M. et al., "Probing the structure-activity relationship of <i>Escherichia coli</i> LT-A by site-directed mutagenesis," <i>Mol. Microbiol.</i> , 1994, 14(1):51-60
C34	PIZZA, M. et al., "The subunit S1 is important for pertussis toxin secretion," <i>J. Biol. Chem.</i> , 1990, 265(29):17759-17763
C35	PRONK, S. et al., "Heat-labile enterotoxin of <i>Escherichia coli</i> ," <i>J. Biol. Chem.</i> , 1985, 260(25):13580-13584
C36	RAPPUOLI, R. et al., "Structure and evolutionary aspects of ADP-ribosylating toxins, <i>Sourcebook of Bacterial Toxins</i> , 1991, Academic Press Limited, 1-21
C37	SANDKVIST, M. et al., "Assembly of <i>Escherichia coli</i> heat-labile enterotoxin and its secretion from <i>Vibrio cholerae</i> ," <i>Molecular Mechanisms of Bacterial Virulence</i> , 1993, Chapter 21, 293-309
C38	SIXMA, T.K. et al., "Crystal structure of a cholera toxin-related heat-labile enterotoxin from <i>E. coli</i> ," <i>Nature</i> , 1991, 351:371-377
C39	SPICER et al., "Sequence homologies between A subunits of <i>Escherichia coli</i> and <i>Vibrio cholerae</i> enterotoxins," <i>Proc. Natl. Acad. Sci. USA</i> , 1981, 78(1):50-54
C40	SPICER et al., " <i>Escherichia coli</i> heat-labile enterotoxin," <i>Biol. Chem.</i> , 1982, 257:5716-5721
C41	TSUJI, T. et al., "A simple amino acid substitution in the A subunit of <i>Escherichia coli</i> enterotoxin results in a loss of its toxic activity," <i>J. Biol. Chem.</i> , 1990, 265:22520-22525
C42	YAMAMOTO, T. et al., "Primary structure of heat-labile enterotoxin produced by <i>Escherichia coli</i> pathogenic for humans," <i>J. Biol. Chem.</i> , 1984, 259:5037-5044
C43	ZOLLER, M. et al., "Oligonucleotide-directed mutagenesis using M13-derived vectors: an efficient and general procedure for the production of point mutations in any fragment of DNA," <i>Nucleic Acids Res.</i> , 1982, 10(20):6487-6500

Examiner Signature		Date Considered	
--------------------	--	-----------------	--

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.